

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant : ANDRIES JAN SMIT  
Serial No. : 10/767,147  
Filing Date : JANUARY 29, 2004  
Docket No. : VOB-34537US1

**AMENDMENT**

Sir:

This Amendment is being filed in response to the Office action mailed June 9, 2010 having a three-month response date of September 9, 2010. Applicant accordingly requests and petitions for a three-month extension of time, up to and including December 9, 2010, within which to respond. Please charge the \$555 extension of time fee and the \$110 fee for one additional independent claim to our Deposit Account No. 16-0820, Order No. VOB-34537US1.

Please amend the application as follows.

## AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-33. (Cancelled).

34. (previously presented) A method according to claim 62, wherein the measured fluorescent radiation is received via a measuring window bounding a surface area, and wherein said portion of the irradiated portion of the skin surface from which the measured fluorescent radiation is received has a surface area larger than the surface area bounded by said measuring window.

35. (previously presented) A method according to claim 34, wherein the surface area of the skin from which the measured fluorescent radiation is received is at least three times larger than the surface area bounded by said measuring window.

36. (currently amended) A method ~~according to claim 32, for determining an advanced glycation/glycosylation end product content of non-locally anomalous, intact skin tissue of a human individual, comprising:~~

using a radiation source to irradiate said skin tissue with electromagnetic excitation radiation;

receiving and measuring an amount of electromagnetic, fluorescent radiation emitted by said skin tissue in response to said irradiation; and

generating, in response to said measured amount of fluorescent radiation, a signal which represents said measured amount of fluorescent radiation; and

determining an advanced glycation/glycosylation end product content of said skin tissue from said signal, and outputting said determined advanced glycation/glycosylation end product content;

wherein said skin tissue is non-locally anomalous, intact skin tissue in vivo which is irradiated noninvasively and simultaneously in its entirety by directing said radiation from said radiation source to a portion of the outer surface of the skin, wherein fluorescent radiation emitted in response to said irradiation is simultaneously received from a surface area of the irradiated portions of the skin surface of at least 1 cm<sup>2</sup>, wherein said fluorescent radiation is received via a measuring window; and wherein said measuring window is oriented at an angle of 25-65° relative to the irradiated portion of the surface of the skin.

37. (currently amended) A method ~~according to claim 32~~, for determining an advanced glycation/glycosylation end product content of non-locally anomalous, intact skin tissue of a human individual, comprising:

using a radiation source to irradiate said skin tissue with electromagnetic excitation radiation;

receiving and measuring an amount of electromagnetic, fluorescent radiation emitted by said skin tissue in response to said irradiation; and

generating, in response to said measured amount of fluorescent radiation, a signal which represents said measured amount of fluorescent radiation; and

determining an advanced glycation/glycosylation end product content of said skin tissue from said signal, and outputting said determined advanced glycation/glycosylation end product content;

wherein said skin tissue is non-locally anomalous, intact skin tissue in vivo which is irradiated noninvasively and simultaneously in its entirety by directing said radiation from said radiation source to a portion of the outer surface of the skin, wherein fluorescent radiation emitted in response to said irradiation is simultaneously received from a surface area of the irradiated portions of the skin surface of at least 1 cm<sup>2</sup>, wherein a supporting structure is held against the skin of the individual, wherein the irradiated skin tissue area is located behind an opening in the supporting structure, wherein the supporting structure supports a measuring window, wherein said fluorescent radiation is received via said measuring window and wherein said measuring window is held at a distance from the skin.

38-48. (cancelled)

49. (previously presented) An apparatus for determining an advanced glycation/glycosylation end product content of non-locally anomalous, intact skin tissue of a human individual, comprising:

a pick-up unit with:

a radiation source, for in vivo and noninvasively irradiating a surface portion of intact skin tissue behind an irradiation window with electromagnetic excitation radiation; and

a detector for measuring an amount of electromagnetic fluorescent radiation received from only a portion of said irradiated skin surface portion;

circuitry connected to said pick-up unit for generating an autofluorescence value for said non-locally anomalous, intact skin tissue in agreement with the measured amount of fluorescent radiation, for determining an advanced glycation/glycosylation end product content of said skin tissue from said signal, and for outputting said determined advanced glycation/glycosylation end product content; and

a measuring window bounding a surface area for passing fluorescent radiation to be detected from said portion of the skin surface from which said amount of fluorescent radiation is received to the detector, said portion of the skin surface from which said amount of fluorescent radiation is received being larger than the surface area bounded by said measuring window.

50. (previously presented) An apparatus according to claim 49, wherein said portion of the skin surface from which said amount of fluorescent radiation is received is at least three times larger than the surface area of said measuring window.

51. (currently amended) An apparatus according to claim 47 for determining an advanced glycation/glycosylation end product content of non-locally anomalous, intact skin tissue of a human individual, comprising:

a pick-up unit with:

a radiation source, for in vivo and noninvasively irradiating intact skin tissue behind an irradiation window with electromagnetic excitation radiation by directing said radiation from said radiation source to a portion to be irradiated of the outer skin surface;  
and

a detector for measuring an amount of electromagnetic fluorescent radiation simultaneously received from a surface area of the irradiated portion of the skin surface of at least 1 cm<sup>2</sup>; and

circuitry connected to said pick-up unit for generating an autofluorescence value for said non-locally anomalous, intact skin tissue in agreement with the measured amount of fluorescent radiation originating from said surface area of said skin tissue, for determining an advanced glycation/glycosylation end product content of said skin tissue from said signal, and for outputting said determined advanced glycation/glycosylation end product content, further comprising a supporting structure to be held against the skin of the individual, for defining a plane in which a surface portion of said skin tissue to be irradiated is located, wherein the supporting structure supports a measuring window for passing light to be detected originating

from said irradiated skin tissue, said measuring window being oriented at an angle of 25-65° relative to said plane and located for receiving radiation emitted from the skin in a direction at an angle to the direction of the excitation radiation.

52. (previously presented) An apparatus according to claim 51, wherein said supporting structure comprises the irradiation window, said measuring window being located adjacent an edge of said irradiation window.

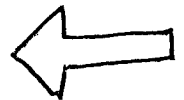
53. (currently amended) An apparatus according to claim 47 for determining an advanced glycation/glycosylation end product content of non-locally anomalous, intact skin tissue of a human individual, comprising:

a pick-up unit with:

a radiation source, for in vivo and noninvasively irradiating intact skin tissue behind an irradiation window with electromagnetic excitation radiation by directing said radiation from said radiation source to a portion to be irradiated of the outer skin surface;  
and

a detector for measuring an amount of electromagnetic fluorescent radiation simultaneously received from a surface area of the irradiated portion of the skin surface of at least 1 cm<sup>2</sup>; and

circuitry connected to said pick-up unit for generating an autofluorescence value for said non-locally anomalous, intact skin tissue in agreement with the measured amount of fluorescent radiation originating from said surface area of said skin tissue, for determining an advanced glycation/glycosylation end product content of said skin tissue from said signal, and for outputting said determined advanced glycation/glycosylation end product content, further comprising a supporting structure to be held against the skin of the individual, for defining a plane in which a surface of said skin tissue to be irradiated is located behind an opening in the supporting structure, wherein the supporting structure supports a measuring window for passing light to be detected originating from said irradiated skin tissue, wherein said measuring window is spaced away from said plane.



54-61. (cancelled)

62. (previously presented) A method for determining an advanced glycation/glycosylation end product content of non-locally anomalous, intact skin tissue of a human individual, comprising:

using a radiation source to irradiate said skin tissue with electromagnetic excitation radiation;

receiving and measuring an amount of electromagnetic, fluorescent radiation emitted by said skin tissue in response to said irradiation; and

generating, in response to said measured amount of fluorescent radiation, a signal which represents said measured amount of fluorescent radiation; and

determining an advanced glycation/glycosylation end product content of said skin tissue from said signal, and outputting said determined advanced glycation/glycosylation end product content;

wherein said irradiated skin tissue is non-locally anomalous, intact skin tissue in vivo which is irradiated noninvasively and simultaneously in its entirety by directing said radiation from said radiation source to a portion of the outer surface of the skin, wherein the measured fluorescent radiation emitted in response to said irradiation is simultaneously received from only a portion of said irradiated portion of said skin surface.

63. (cancelled)

64. (previously presented) A method according to claim 62, wherein the measured fluorescent radiation has one or more wavelengths larger than 420 nm.

65. (cancelled)

66. (previously presented) An apparatus for determining an advanced glycation/glycosylation end product content of non-locally anomalous, intact skin tissue of a human individual, comprising:

a pick-up unit with:

a radiation source, for in vivo and noninvasively irradiating intact skin tissue behind an irradiation window by directing electromagnetic excitation radiation from said radiation source to a portion of the outer skin surface behind the irradiation window; and

a detector for measuring an amount of electromagnetic fluorescent radiation emitted in response to said irradiation received simultaneously from only a portion of said irradiated skin surface portion; and

circuitry connected to said pick-up unit for generating an autofluorescence value for said non-locally anomalous, intact skin tissue in agreement with a measured amount of fluorescent

radiation originating from said portion of said irradiated portion of said skin surface, for determining an advanced glycation/glycosylation end product content of said skin tissue from said signal, and for outputting said determined advanced glycation/glycosylation end product content.

67. (previously presented) A method according to claim 62, wherein the size of the portion of the irradiated skin surface portion from which the measured fluorescent radiation is received is at least 1 cm<sup>2</sup>.

68. (previously presented) An apparatus according to claim 66, wherein the detector is arranged for measuring electromagnetic fluorescent radiation received from a surface area of said portion of said irradiated skin surface portion of at least 1 cm<sup>2</sup>.

69. (previously presented) A method for determining an advanced glycation/glycosylation end product content for a human individual, comprising:

irradiating skin tissue of said individual with electromagnetic excitation radiation;

receiving and measuring an amount of electromagnetic, fluorescent radiation emitted by said material in response to said irradiation; and

generating, in response to said measured amount of fluorescent radiation, a signal which represents a determined advanced glycation/glycosylation end product content for said individual;

wherein said skin tissue is non-locally anomalous, intact skin tissue in vivo of which a surface is irradiated noninvasively and simultaneously in its entirety;

wherein fluorescent radiation emitted in a direction at an angle to the direction of the excitation radiation is simultaneously received from different portions of the skin surface;

wherein said fluorescent radiation is received via a measuring window; and

wherein said measuring window is oriented at an angle of 25-65° relative to the irradiated surface of the skin.

70. (previously presented) A method for determining an advanced glycation/glycosylation end product content for a human individual, comprising:

irradiating skin tissue of said individual with electromagnetic excitation radiation via an opening in a surface contacting the skin;

receiving and measuring an amount of electromagnetic, fluorescent radiation emitted by said material in response to said irradiation; and

generating, in response to said measured amount of fluorescent radiation, a signal which represents a determined advanced glycation/glycosylation end product content for said individual;

wherein said skin tissue is non-locally anomalous, intact skin tissue in vivo of which a surface is irradiated noninvasively and simultaneously in its entirety;

wherein fluorescent radiation emitted in response to said irradiation is simultaneously received from different portions of the skin surface; and

wherein said fluorescent radiation is received via a measuring window and wherein said measuring window is held at a distance from the skin.

71. (previously presented) An apparatus for determining an advanced glycation/glycosylation end product content for a human individual, comprising:

a pick-up unit with:

a radiation source, for in vivo and noninvasively irradiating a surface of non-locally anomalous, intact skin tissue with electromagnetic excitation radiation via an irradiation window for delimiting a surface portion of said skin tissue to be irradiated; and

a detector for measuring an amount of electromagnetic fluorescent radiation received from a surface area of said skin tissue in a direction at an angle to the direction of the excitation radiation;

circuitry connected to said pick-up unit for generating a value representing a determined advanced glycation/glycosylation end product content for said individual in agreement with the measured amount of fluorescent radiation originating from said surface area of said skin tissue; and

a supporting structure to be held against the skin of the individual, for defining a plane in which a surface portion of said skin tissue to be irradiated is located;

wherein the supporting structure supports a measuring window for passing light to be detected from said irradiated skin tissue, said measuring window being oriented at an angle of 25-65° relative to said plane.

72. (previously presented) An apparatus for determining an advanced glycation/glycosylation end product content for a human individual, comprising:

a pick-up unit with:



a radiation source, for in vivo and noninvasively irradiating a surface of non-locally anomalous, intact skin tissue behind an irradiation window with electromagnetic excitation radiation in a direction perpendicular to the skin; and

a detector for measuring an amount of electromagnetic fluorescent radiation received from a surface area of said skin tissue;

circuitry connected to said pick-up unit for generating a value representing a determined advanced glycation/glycosylation end product content for said individual in agreement with the measured amount of fluorescent radiation originating from said surface area of said skin tissue; and

a supporting structure to be held against a skin of the individual, for defining a plane in which said surface of said skin tissue to be irradiated is located behind an opening in the supporting structure, wherein the supporting structure supports a measuring window for passing light to be detected coming from said irradiated skin tissue, wherein said measuring window is spaced away from said plane.

73. (previously presented) A method according to claim 62, wherein the fluorescent radiation emitted in response to said irradiation is simultaneously received from a surface area of the irradiated portion of the skin surface larger than  $0.1 \text{ cm}^2$ .

74. (previously presented) An apparatus according to claim 66, wherein the surface area of the irradiated portion of the skin surface from which the fluorescent radiation emitted in response to said irradiation can be received simultaneously is larger than  $0.1 \text{ cm}^2$ .

## REMARKS

Applicant's counsel thanks the Examiner for the careful consideration given the application. In the Office action, the Examiner rejected claims 34, 35, 62, 64, 66-68, 73 and 74 only under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. More specifically, the claims have been rejected on the grounds that the specification does not disclose that measured radiation is emitted in response to irradiation received from only a portion of an irradiated portion of a skin surface, referring to page 8, lines 4-8 and page 11, lines 6-7 of the specification as originally filed. However, in the specification, at page 7, lines 25-29 a preference is described for providing that: *"the surface 23 of the skin 7 within the irradiation window 8 from where light can be received by the fiber via the measuring window 18 is preferably greater than 0.1 cm<sup>2</sup> and in particular 1-4 cm<sup>2</sup>, but smaller than the irradiation window and hence smaller than the irradiated surface of the skin 7."* (emphasis added.)

Clearly, the area of the skin behind the irradiation window constitutes the irradiated portion of the skin surface. It is thus explicitly described that preferably the surface of the skin from where light can be received is smaller than the irradiated portion of the skin surface.

Regarding claims 67 and 68 the objection was raised that the description does not describe that the skin surface portion from which fluorescent radiation can be received can be 1 cm<sup>2</sup>. While this appears correct for page 7, lines 25-29 (greater than 1-4 cm<sup>2</sup>), it is disclosed at page 8, lines 9-10 that the skin surface to be measured (measuring involving receiving radiation) is preferably 1 to 4 cm<sup>2</sup>, so the 1 cm<sup>2</sup> value is described.

In view of the foregoing, it is clear that the subject matter of the specified claims is sufficiently described in the specification so that the requirements of 35 U.S.C. 112, first paragraph, are met.

In paragraph 9 of the Office action, the Examiner stated that claims 36, 37 and 51-53 would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims. Applicant has decided to accept the Examiner's suggestion. Accordingly, these claims have now been rewritten in independent form including all the limitations of the base claim and any intervening claims.

In paragraph 10 of the Office action, the Examiner stated that claims 49, 50 and 69-72 are allowed. Applicant has accordingly maintained these claims in the case.

All the other claims in the case (claims 32, 38-40, 43-45, 47-48, 54-58, 60, 61 and 65) have been cancelled without prejudice.

In summary, what applicant is doing in this Amendment is as follows. Claims 34, 35, 62, 64, 66-68, 73 and 74 were rejected only under Section 112, first paragraph (and not based on Section 102 or 103); for the reasons set forth above, these claims satisfy the written description requirement and accordingly are now in condition for allowance. Next, applicant has elected to retain the claims which the Examiner stated are allowable (these being claims 36, 37, 49, 50, 51-53, and 69-72). All the other claims in the case (that is, all the claims rejected based on Sections 102 and 103) have been cancelled without prejudice.

Since all open items have now been resolved, it is clear that a Notice of Allowance is now in order and is respectfully requested. If any further fees are required by this communication, please charge such fees to our Deposit Account No. 16-0820, Order No. VOB-34537US1.

Respectfully submitted,  
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